Fundamental Limits of Predicting Epidemic Outbreaks

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Abstract

During the outbreak of a virus, perhaps the greatest concern is the future evolution of the epidemic: *How many people will be infected and which regions will be affected the most?* The accurate prediction of an epidemic enables targeted disease counter-measures (e.g., allocating medical staff and quarantining). This work considers fundamental limits for the prediction of an epidemic. More precisely, we demonstrate the ill-conditioning of predicting the logistic function, which is central to epidemic models. Small modelling and measurement errors tremendously deteriorate the prediction accuracy. Thus, a real-world epidemic outbreak can be predicted reliably only in the short term.

1 Introduction

The vast majority of epidemic models assumes that every individual is in either one compartment [1]. Every compartment describes another stage of the disease. The two most fundamental compartments are *susceptible* (healthy) and *infected*. Susceptible individuals can get infected by contact with infectious individuals. Conceptually, there are two kinds of compartmental epidemic models. First, the Susceptible-Infected-Susceptible (SIS) epidemic model assumes that infected individuals can cure and become infected again.

Definition 1 (Susceptible-Infected-Susceptible (SIS) Epidemic Model)**.** *Consider a population with M individuals, which are either susceptible or infected at every time $t \geq 0$. Denote the infection rate by $\beta > 0$ and the curing rate by $\delta > 0$. Then, the number of infected individuals $\mathcal{I}(t)$ evolves according to*

$$\frac{d\mathcal{I}(t)}{dt} = \frac{\beta}{M}\mathcal{S}(t)\mathcal{I}(t) - \delta\mathcal{I}(t),$$

and the number of susceptible individuals follows as $\mathcal{S}(t) = M - \mathcal{I}(t)$.

The Susceptible-Infected-Removed (SIR) model is the second kind of compartmental epidemic models. The SIR model assumes that cured individuals are immune to the disease, which is modelled by the *removed* compartment.

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Definition 2 (Susceptible-Infected-Removed (SIR) Epidemic Model)**.** *Consider a population with M individuals, which are either susceptible or infected or removed at every time $t \geq 0$. Denote the infection rate by $\beta > 0$ and the curing rate by $\delta > 0$. Then, the number of infected individuals $\mathcal{I}(t)$ evolves according to*

$$\frac{d\mathcal{I}(t)}{dt} = \frac{\beta}{M}\mathcal{S}(t)\mathcal{I}(t) - \delta\mathcal{I}(t),$$

the number of removed individuals $\mathcal{R}(t)$ evolves according to

$$\frac{d\mathcal{R}(t)}{dt} = \delta\mathcal{I}(t), \tag{1}$$

and the number of susceptible individuals follows as $\mathcal{S}(t) = M - \mathcal{I}(t) - \mathcal{R}(t)$.

There are variations to both the SIS and the SIR model [1]. For instance, the Susceptible-Infected-Removed-Susceptible (SIRS) model and the Susceptible-Exposed-Infected-Removed (SEIR) model, which consider time-limited immunity and an incubation period, respectively. In this work, we focus on the basic SIS and SIR models. For both models, we consider the prediction of the future evolution of the epidemic at times $t \geq t_{\text{obs}}$, given observations of the compartments until some observation time t_{obs}. In this work, we argue that the prediction of an epidemic is ill-conditioned, which is a property that is independent of the particular prediction algorithm.

2 The Logistic Function in Epidemic Models

At the heart of both the SIS and the SIR epidemic model lies the logistic function $f(t)$, which is given by

$$f(t) = \frac{y_\infty}{1 + e^{-K(t-t_0)}}. \tag{2}$$

Here, we denote the *steady-state* by $y_\infty > 0$, the *inflection point* by t_0 and the logistic *growth rate* by $K > 0$. Furthermore, we denote the *scaled* inflection point by $\tilde{t}_0 = Kt_0$. For both the SIS and the SIR epidemic model, we denote the *effective infection rate* by $\tau = \beta/\delta$. Proposition 3 states that the solution of the SIS model is given by a logistic function. Proposition 3 is not a novel contribution but included for completeness.

Proposition 3. *Consider the SIS epidemic model and assume that $\beta > \delta$ and $\mathcal{I}(0) > 0$. Then, the number of infected individuals $\mathcal{I}(t)$ is given by a logistic curve*

$$\mathcal{I}(t) = \frac{M}{1 + e^{-K(t-t_0)}}\left(1 - \frac{1}{\tau}\right).$$

Here, the logistic growth rate equals $K = \beta - \delta$, and the inflection point equals

$$t_0 = \frac{1}{K}\log\left(\frac{M}{\mathcal{I}(0)}\left(1 - \frac{1}{\tau}\right) - 1\right).$$

Also for the SIS epidemic model *on networks*, the logistic curve gives an approximation and bounds for describing the number of infected individuals [2, 3].

Similarly to Proposition 3, in the SIR epidemic model, the solution for the removed compartment $\mathcal{R}(t)$ can be approximated by a logistic function, as shown in the seminal work of Kermack and McKendrick [4].

Proposition 4 ([4]). *Consider the SIR epidemic model and assume that $\mathcal{R}(0) = 0$ and $\mathcal{I}(0) > 0$. Then, if $\mathcal{R}(t) << \delta/\beta$ holds true at all times t, the number of removed individuals $\mathcal{R}(t)$ can be approximated by a logistic curve at all times $t \geq 0$ as*

$$\mathcal{R}(t) \approx Mr_1 + M\frac{r_2 - r_1}{1 - \frac{r_2}{r_1}e^{-\frac{1}{2}\tau^2(r_2-r_1)\tilde{t}}}.$$

Here, the constants r_1 and r_2 equal to

$$r_l = \begin{cases} \frac{1}{s_0\tau^2}\left((s_0\tau - 1) + \sqrt{(s_0\tau-1)^2 + 2s_0(1-s_0)\tau^2}\right) & \text{if} \quad l = 1, \\ \frac{1}{s_0\tau^2}\left((s_0\tau - 1) - \sqrt{(s_0\tau-1)^2 + 2s_0(1-s_0)\tau^2}\right) & \text{if} \quad l = 2. \end{cases}$$

More precisely, Proposition 4 states that the removed individuals $\mathcal{R}(t)$ is approximated by a logistic function *plus the offset* Mr_1. By the definition of the SIR model in (1), the number of infection $\mathcal{I}(t)$ is proportional to the derivative of the removed individuals $\mathcal{R}(t)$. Thus, Proposition 4 implies that the *cumulative* number of infections

$$\mathcal{I}_c(t) = \int_0^t \mathcal{I}(z)\, dz \tag{3}$$

is approximated by a logistic function (plus offset). Then, the peak of the epidemic, i.e., the largest *increase* of infections, occurs at the inflection point t_0.

3 Prediction of Epidemic Outbreaks

Proposition 3 and Proposition 4, and variations thereof, motivate the application of the logistic function (2) to the prediction of an epidemic outbreak. In particular, the logistic function has been applied to forecast the Coronavirus Virus Disease 2019 (Covid-19) outbreak in China [5, 6, 7, 8, 9], The Netherlands [10] and Italy [11]. We consider the prediction of the cumulative number of infections $\mathcal{I}_c(t)$, as defined in (3). In a real-world epidemic, the infections $\mathcal{I}_c(t)$ does not exactly follow a logistic function $f(t)$. Instead, the infections $\mathcal{I}_c(t)$ satisfy

$$\mathcal{I}_c(t) = f(t) + w(t) \tag{4}$$

for some logistic function $f(t)$ and the unknown *model error* $w(t)$. Real-world epidemic data is collected in a periodic manner. For instance, the RIVM reports the number of Covid-19 infections in the Netherlands on a daily basis. We assume that the cumulative number of infections $\mathcal{I}_c(t)$ has been observed at the discrete times $t = 1, 2, ..., t_{\text{obs}}$, where $t_{\text{obs}} \in \mathbb{N}$ denotes the *observation time*.

To predict the number of infections $\mathcal{I}_c(t)$ at times $t > t_{\text{obs}}$, we consider a two-step approach. First, we obtain parameter estimates $\hat{y}_\infty, \hat{t}_0, \hat{K}$ of the logistic function $f(t)$ by solving the non-linear least-squares problem

$$(\hat{y}_\infty, \hat{t}_0, \hat{K}) = \underset{y_\infty, t_0, K}{\operatorname{argmin}} \sum_{t=1}^{t_{\text{obs}}} \left(\mathcal{I}_c(t) - \frac{y_\infty}{1 + e^{-K(t-t_0)}}\right)^2. \tag{5}$$

Second, we predict the number of infections $\mathcal{I}_c(t)$ at times $t > t_{\text{obs}}$ by the logistic function (2) as $\hat{\mathcal{I}}_c(t) \approx \hat{f}(t)$, where the estimate of the logistic function $f(t)$ equals

$$\hat{f}(t) = \frac{\hat{y}_\infty}{1 + e^{-\hat{K}(t-\hat{t}_0)}}.$$

The remainder of this section consists of two parts. First, we focus on the simplified problem of fitting the logistic function $f(t)$ to three points in Subsection 3.1. Second, we argue that the prediction of epidemics is ill-conditioned in Subsection 3.2.

3.1 Fitting the Logistic Function to Three Equidistant Points

The logistic function $f(t)$ can be fitted to three equidistant points in closed-form, as stated by Proposition 5.

Proposition 5. *Consider three points $y_3 > y_2 > y_1 > 0$ and a time spacing Δt. Define the* growth metric *as*

$$\Phi\left(y_1, y_2, y_3\right) = \frac{y_2}{y_3} - \frac{y_1}{y_2}. \tag{6}$$

Then, there exists a logistic function $f(t)$ with $f(0) = y_1$, $f(\Delta t) = y_2$ and $f(2\Delta t) = y_3$ if and only if

$$\Phi\left(y_1, y_2, y_3\right) > 0. \tag{7}$$

Furthermore, the logistic function $f(t)$ is unique, and the steady-state equals

$$y_\infty = y_1 + \frac{\left(y_1 - y_2\right)^2}{y_2} \frac{1}{\Phi(y_1, y_2, y_3)}, \tag{8}$$

the logistic growth rate equals

$$K = -\frac{1}{\Delta t} \log\left(\frac{y_1}{y_2} + \frac{y_1}{y_1 - y_2}\Phi\left(y_1, y_2, y_3\right)\right), \tag{9}$$

and the inflection point equals

$$t_0 = \frac{1}{K} \log\left(\frac{\left(y_1 - y_2\right)^2}{y_1 y_2} \frac{1}{\Phi(y_1, y_2, y_3)}\right). \tag{10}$$

Proof. Appendix B. □

To state the closed-form expressions for the parameters y_∞, K, t_0, we defined the *growth metric* $\Phi\left(y_1, y_2, y_3\right)$ in (6). The growth metric $\Phi\left(y_1, y_2, y_3\right)$ seems to be a central quantity for fitting the logistic function $f(t)$. If $y_1 = g(t)$, $y_2 = g(\Delta t)$ and $y_3 = g(2\Delta t)$ for some function $g(t)$, then the growth metric $\Phi\left(y_1, y_2, y_3\right)$ is related to the second derivative of the function $h(t) = -\log\left(g(t)\right)$. The first derivative of $h(t)$ equals $h'(t) = -g'(t)/g(t)$. Applying Euler's method to $h'(t)$ with sampling time Δt gives

$$h''(t) \approx -\frac{1}{\Delta t}\left(\frac{g'\left(t + \Delta t\right)}{g\left(t + \Delta t\right)} - \frac{g'(t)}{g(t)}\right).$$

Applying Euler's method to both $g'\left(t + \Delta t\right)$ and $g'(t)$ yields that

$$h''(t) \approx -\frac{1}{\Delta t^2}\left(\frac{g\left(t + \Delta t\right) - g\left(t\right)}{g\left(t + \Delta t\right)} - \frac{g\left(t\right) - g\left(t - \Delta t\right)}{g(t)}\right).$$

Hence, by identifying $y_1 = g\left(t - \Delta t\right)$, $y_2 = g\left(t\right)$ and $y_3 = g\left(t + \Delta t\right)$, it holds that

$$\Phi\left(y_1, y_2, y_3\right) \approx \Delta t^2 h''(t).$$

If the points y_1, y_2, y_3 lie on a logistic function $f(t)$, then we can express the growth metric $\Phi\left(y_1, y_2, y_3\right)$ as a power series:

Proposition 6 (Power Series for the Growth Metric)**.** *For some logistic function $f(t)$ and time spacing Δt, consider three values $y_1 = f(0)$, $y_2 = f(\Delta t)$ and $y_3 = f(2\Delta t)$. Furthermore, denote the* scaled *time spacing as $\Delta\tilde{t} = K\Delta t$. Then, for a sufficiently small*[1] *time spacing $\Delta\tilde{t}$, the growth metric can be expressed as*

$$\Phi\left(y_1, y_2, y_3\right) = \frac{1}{1+e^{\tilde{t}_0}} \sum_{n=2}^{\infty} \left(\Delta\tilde{t}\right)^n \left(\frac{(-1)^n}{n!} - \left(1+e^{\tilde{t}_0}\right) c_n \right). \tag{11}$$

Here, the coefficients c_n are recursively defined as $c_0 = 1$ and

$$c_n = -\frac{1}{e^{\tilde{t}_0}+1} \sum_{l=0}^{n-1} c_l \frac{1}{(n-l)!}, \quad n \geq 1.$$

Proof. Appendix A. □

Figure 1 shows that the growth rate $\Phi(f(0), f(t/2), f(t))$ is close to zero for all times $t < t_0$ for an exemplary logistic function $f(t)$ with parameters $K = 0.5$, $t_0 = 10$ and $y_\infty = 1$.

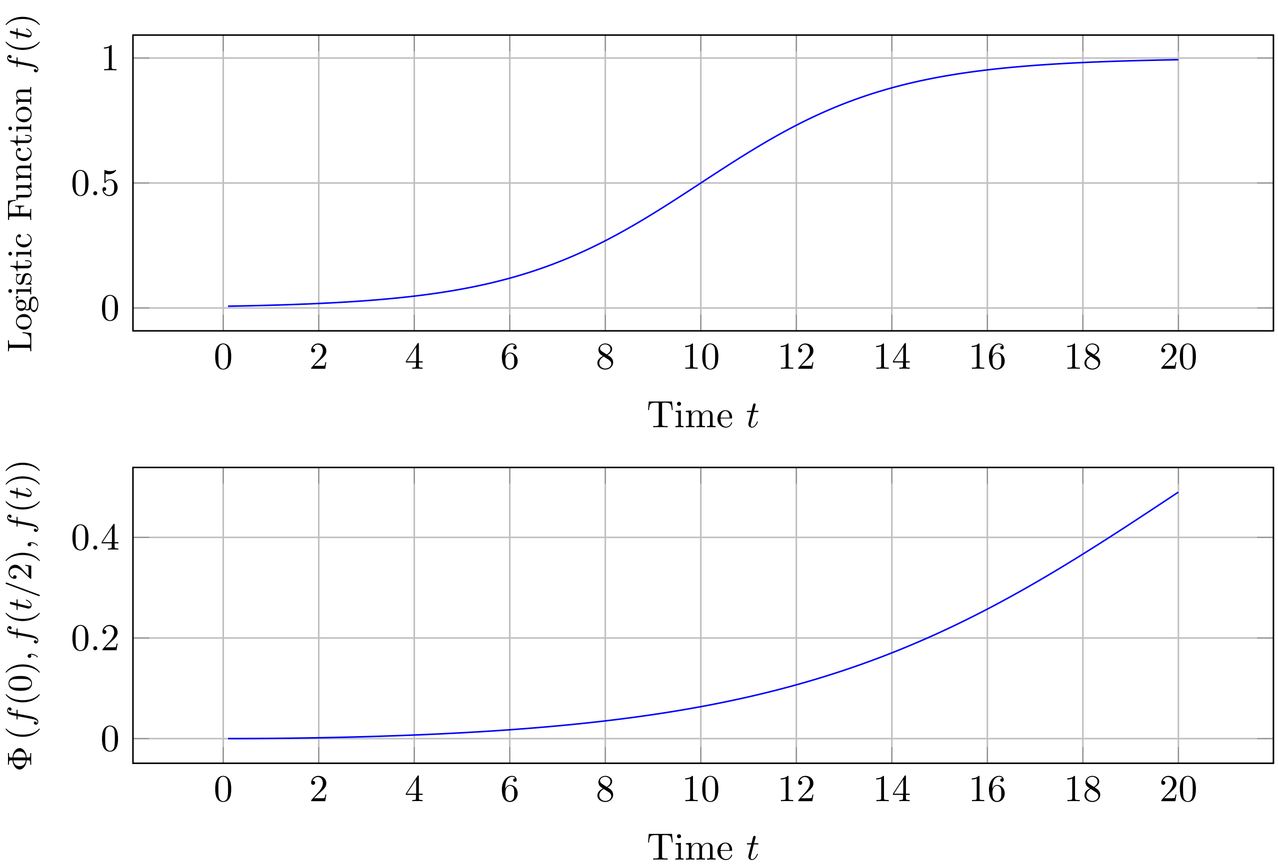

Figure 1: **Growth metric for a logistic function.** Upper subplot: The logistic function $f(t)$ versus time t. Lower subplot: The growth metric $\Phi(y_1, y_2, y_3)$ for the points $y_1 = f(0)$, $y_2 = f(t/2)$, $y_3 = f(t)$ versus time t.

[1] Numerical simulations seem to indicate that the power series (11) converges for all time spacings $\Delta\tilde{t}$. The analytical derivation of the radius of convergence of the power series (11) is an open problem.

3.2 Ill-Conditioning of Predicting Epidemic Outbreaks

If the model errors $w(t)$ in (4) are sufficiently small, then the solution $\hat{y}_\infty, \hat{t}_0, \hat{K}$ to the least-squares problem (5) approximately equals to the true parameters y_∞, t_0, K. However, it is not clear what "sufficiently small" means. Thus, we face the fundamental question: *How much do small, but non-zero, model errors $w(t)$ affect the accuracy of the estimate $\hat{f}(t)$?*

To quantify the deviation of the estimated logistic function $\hat{f}(t)$ to the true function $f(t)$, we apply Proposition 5, which states that every logistic function can be parameterised by specifying three points y_1, y_2 and y_3. We choose three points y_1, y_2 and y_3 in the observation time interval $[0, t_{\text{obs}}]$. More precisely, we set the three points of the true logistic function $f(t)$ in (4) to $y_1 = f(0)$, $y_2 = f(t_{\text{obs}}/2)$ and $y_3 = f(t_{\text{obs}})$. Analogously, we denote the corresponding points of the estimate $\hat{f}(t)$, obtained by (5), as $\hat{y}_1 = \hat{f}(0)$, $\hat{y}_2 = \hat{f}(t_{\text{obs}}/2)$ and $\hat{y}_3 = \hat{f}(t_{\text{obs}})$. The points $\hat{y}_1, \hat{y}_2, \hat{y}_3$ depend on the unknown model error $w(t)$. If the model error $w(t) \to 0$ at every time $t \in [0, t_{\text{obs}}]$, then it holds that $\hat{y}_i \to y_i$ for $i = 1, 2, 3$, which implies that $\hat{f}(t) \to f(t)$ at every time t.

We consider the *best-case* and assume that, due to non-zero model errors $w(t)$, the estimate $\hat{f}(t)$ differs from the true function $f(t)$ in only one of the points y_1, y_2, y_3. More precisely, we consider that $\hat{y}_1 = y_1$, $\hat{y}_2 = y_2$ and $\hat{y}_3 = y_3 + \epsilon$ for some small $\epsilon > 0$. Thus, $\epsilon \downarrow 0$ implies that $\hat{f}(t) \to f(t)$ at every time t. For now, we focus on the sensitivity of estimating the steady state y_∞. We define $\hat{y}_\infty(\epsilon)$ as the estimate of the steady state y_∞, given the perturbation $\hat{y}_3 = y_3 + \epsilon$. By applying Taylor's Theorem to (8), we obtain for a small $\epsilon > 0$ that

$$\hat{y}_\infty(\epsilon) = y_\infty + \epsilon \kappa_1(t_{\text{obs}}) + \mathcal{O}\left(\epsilon^2\right), \tag{12}$$

where we define[2] the *condition number* $\kappa_1(t_{\text{obs}})$ as

$$\kappa_1(t_{\text{obs}}) = \frac{\partial}{\partial y_3}\left(y_1 + \frac{(y_1 - y_2)^2}{y_2} \frac{1}{\Phi(y_1, y_2, y_3)} \right). \tag{13}$$

The condition number $\kappa_1(t_{\text{obs}})$ depends on the observation time t_{obs}, since the three points are given by $y_1 = f(0)$, $y_2 = f(t_{\text{obs}}/2)$ and $y_3 = f(t_{\text{obs}})$. From (12) it follows that the condition number $\kappa_1(t_{\text{obs}})$ describes the impact, or the amplification, of a small error $\epsilon = \hat{y}_3 - y_3$ on the estimate $\hat{y}_\infty(\epsilon)$. *The greater the condition number $\kappa_1(t_{obs})$, the harder it is to estimate the steady state y_∞.* Analogously to the condition number $\kappa_1(t_{\text{obs}})$ for the estimate of the steady state $y_\infty(\epsilon)$, we define the condition numbers $\kappa_2(t_{\text{obs}})$ and $\kappa_3(t_{\text{obs}})$ for the growth rate estimate $\hat{K}(\epsilon)$ and the inflection point estimate $\hat{t}_0(\epsilon)$, respectively. (See also Appendix C.)

Proposition 7 (Condition Numbers of Estimating the Logistic Function Parameters)**.** *Consider three points $y_1 = f(0)$, $y_2 = f(t_{\text{obs}}/2)$ and $y_3 = f(t_{\text{obs}})$ on the logistic function $f(t)$. With respect to a small perturbation ϵ of the point y_3, the condition number of the steady-state estimate $\hat{y}_\infty(\epsilon)$ equals*

$$\kappa_1(t_{\text{obs}}) = \frac{(y_1 - y_2)^2}{y_3^2} \frac{1}{\Phi^2(y_1, y_2, y_3)}, \tag{14}$$

[2] For a matrix A, the most common definition of the condition number is $\kappa(A) = \sigma_{\max}/\sigma_{\min}$, where $\sigma_{\max}$ and $\sigma_{\min}$ denote the greatest and smallest singular value of the matrix A. Analogously to (13), the condition number $\kappa(A)$ describes the sensitivity the solution x of the linear system $Ax = b$, when the vector b is perturbed [12].

the condition number of the growth-rate estimate $\hat{K}(\epsilon)$ *equals*

$$\kappa_2(t_{\text{obs}}) = \frac{2}{t_{\text{obs}}} \frac{y_2^2}{y_3^2} \frac{1}{y_1 - y_2 + y_2 \Phi\left(y_1, y_2, y_3\right)}, \tag{15}$$

and the condition number of the inflection-point estimate $\hat{t}_0(\epsilon)$ *equals*

$$\kappa_3(t_{\text{obs}}) = \frac{1}{K} \frac{y_2}{y_3^2} \left(\frac{1}{\Phi(y_1, y_2, y_3)} - \frac{2t_0 y_2}{t_{\text{obs}}} \frac{1}{y_1 - y_2 + y_2 \Phi\left(y_1, y_2, y_3\right)} \right). \tag{16}$$

Proof. Appendix C. □

Proposition 7 shows that the growth metric $\Phi\left(y_1, y_2, y_3\right)$ is a central quantity in assessing the difficulty of estimating the parameters y_∞, K, t_0. We consider an exemplary logistic function $f(t)$ with parameters $K = 0.5$, $t_0 = 10$ and $y_\infty = 1$. Figure 2 shows that the condition numbers $\kappa_1(t)$, $\kappa_2(t)$, and $\kappa_3(t)$ are very large. For instance at time $t = 5 = t_0/2$, the magnitude of the condition number $|\kappa_1(5)|$ is greater than 100. Thus, the steady-state estimate $\hat{y}_\infty(\epsilon)$ is distorted by the error ϵ times a factor of 100. Furthermore, Figure 2 indicates that the estimation of the growth rate parameter K is most robust against model errors $w(t)$, since the condition number $\kappa_2(t)$ is the smallest.

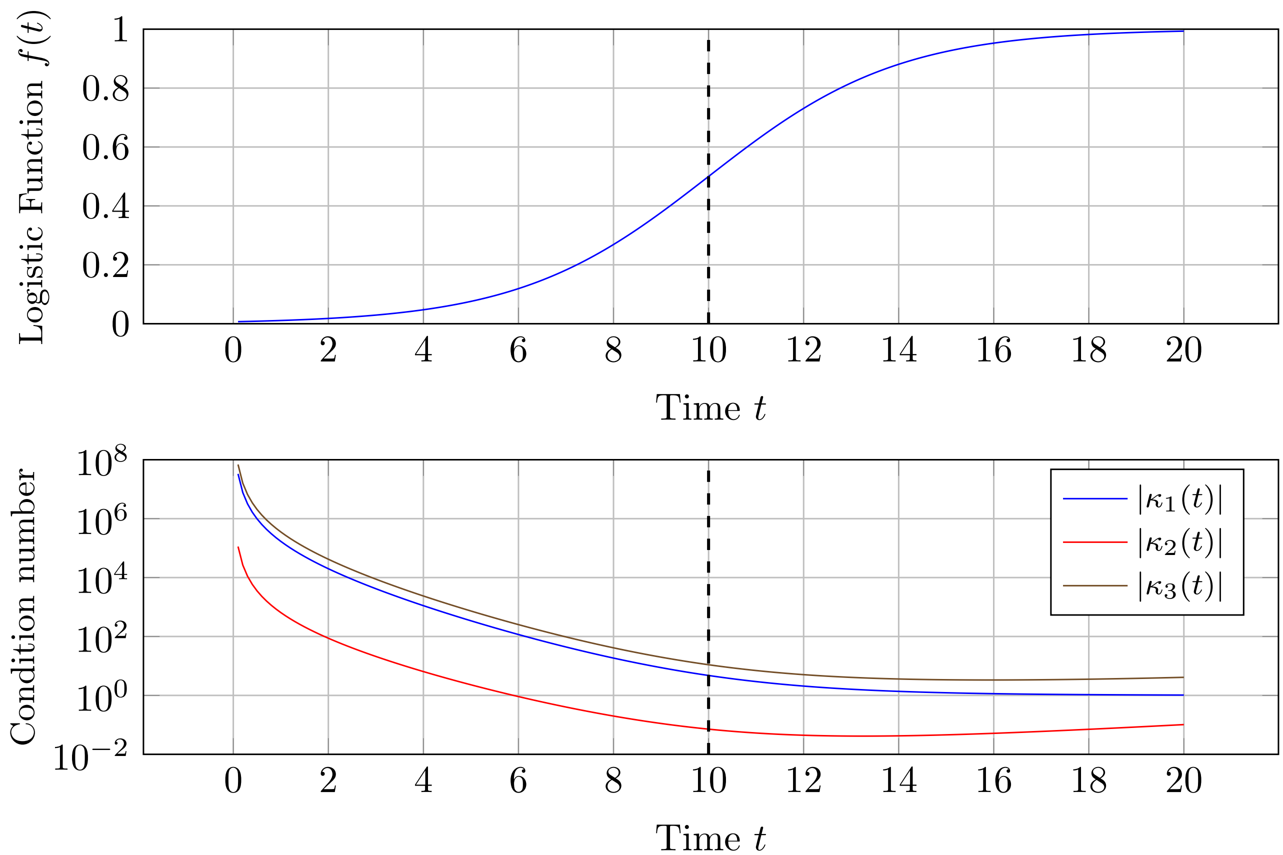

Figure 2: **Condition numbers of estimating the parameters of a logistic function.** Upper subplot: The logistic function $f(t)$ versus time t. Lower subplot: The absolute value of the condition numbers $\kappa_1(t)$, $\kappa_2(t)$, and $\kappa_3(t)$ versus time t on a semi-logarithmic plot. The dashed line indicates the inflection point $t_0 = 10$.

We emphasise that, for simplicity, Proposition 7 considers the best case: the perturbation of only one point y_3. If the points y_1 and y_2 are also perturbed, then the condition numbers become even greater than the expressions in Proposition 7. Nevertheless, the best-case scenario in Proposition 7 suffices to show that the estimation of the logistic function parameters y_∞, K, t_0 is ill-conditioned for small observation times t_{obs}:

Proposition 8 (Ill-Conditioning of Estimating the Logistic Function Parameters)**.** *Consider three points $y_1 = f(0)$, $y_2 = f(t_{\text{obs}}/2)$ and $y_3 = f(t_{\text{obs}})$ on the logistic function $f(t)$. With respect to a small perturbation ϵ of the point y_3, it holds that*

$$\frac{1}{\kappa_i(t_{\text{obs}})} = \mathcal{O}\left(t_{\text{obs}}^2\right)$$

as $t_{\text{obs}} \downarrow 0$ for all $i = 1, 2, 3$.

Proof. Appendix D. □

Proposition 8 states that, for estimating the logistic function parameters y_∞, K, t_0, the condition numbers $\kappa_i(t_{\text{obs}})$ are very large for a small observation time t_{obs}. For every real-world epidemic outbreak, there are significant non-zero model errors $w(t)$. Thus, Proposition 8 implies that an accurate prediction of the logistic function $f(t)$ is impossible in practice, unless the epidemic has been observed for a long time t_{obs}.

4 Numerical Simulations

We perform numerical simulations to illustrate the sensitivity of predicting an epidemic outbreak subject to model errors $w(t)$. We generate the model errors $w(t)$ in (4) as Gaussian random variables with zero mean and standard deviation σ. The model errors $w(t)$ and $w(\tilde{t})$ are stochastically independent for all times $t \neq \tilde{t}$. If the cumulative number of infections $\mathcal{I}_c(t)$, resulting from (4), is negative,then we set $\mathcal{I}_c(t) \leftarrow |\mathcal{I}_c(t)|$. Figure 3 shows the prediction results for three scenarios: small model errors ($\sigma = 2 \cdot 10^{-4}$); large model errors ($\sigma = 10^{-3}$); and the number of Covid-19 infections $\mathcal{I}_c(t)$ in the Netherlands. Small model errors $w(t)$ have a great impact on the accuracy of the estimated number of infections $\hat{I}_c(t)$ and the inflection-point estimate $\hat{t}_0$. The prediction of the number of infections $I_c(t)$ is accurate only in the short term.

5 Conclusions

For many epidemic models, the (cumulative) number of infections is given by a logistic function, at least approximately. In this work, we showed that the prediction of a logistic function is ill-conditioned. More specifically, a good fit of a logistic function $\hat{f}(t)$ to the epidemic data until some observation time t_{obs} does *not* imply that the function $\hat{f}(t)$ yields accurate predictions at times $t > t_{\text{obs}}$. Hence, even under idealised conditions, the prediction of an epidemic is inherently difficult, regardless of the particular prediction algorithm.

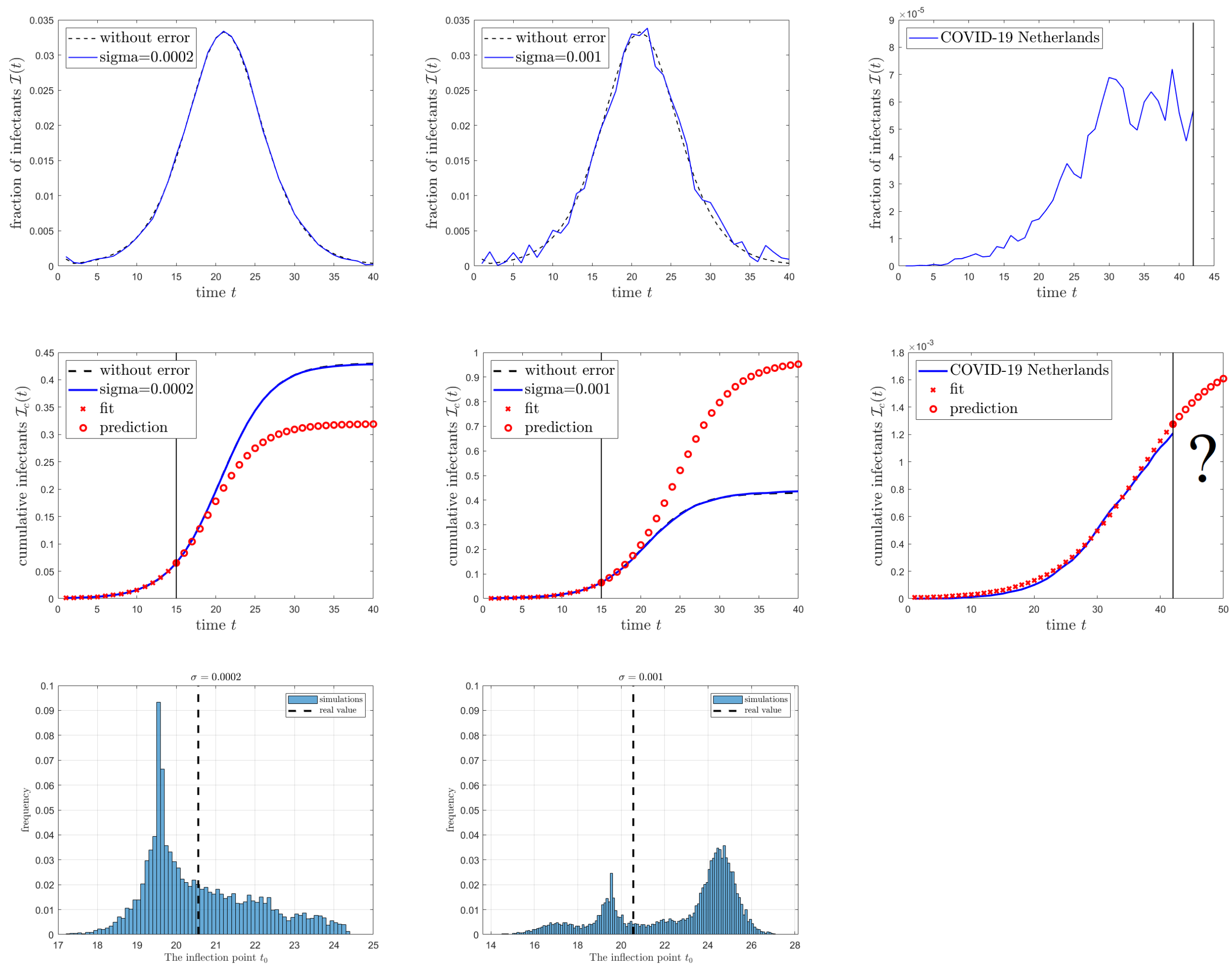

Figure 3: **Sensitivity of predicting an epidemic outbreak.** The first and second column correspond to the logistic function (4) plus Gaussian model errors $w(t)$ with a standard deviation of $\sigma = 2 \cdot 10^{-4}$ and $\sigma = 10^{-3}$, respectively. The parameters of the logistic function $f(t)$ are $t_0 = 20.5, K = 0.31$ and $y_\infty = 0.43$. The third column shows the cumulative number of Covid-19 infections in the Netherlands (up to March 29). The first row shows the (non-cumulative) number of infections $\mathcal{I}(t)$ versus time t, and the vertical line indicates the observation time t_{obs}. The second row shows the cumulative number of infections $\mathcal{I}_c(t)$ and the predicted value $\hat{\mathcal{I}}_c(t)$. The third row depicts the histograms of the inflection-point estimate $\hat{t}_0$, which has been obtained by repeating the simulations in the top two rows for 10,000 times. The real inflection point t_0 is shown by a dashed line.

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A Proof of Proposition 6

Since $y_1 = f(0)$, $y_2 = f(\Delta t)$ and $y_3 = f(2\Delta t)$, we obtain from the definition of the logistic function $f(t)$ in (2) that

$$\frac{y_1}{y_2} = \frac{y_\infty}{1 + e^{Kt_0}} \frac{1 + e^{K(t_0 - \Delta t)}}{y_\infty}.$$

Thus, it holds with $\tilde{t}_0 = Kt_0$ and $\Delta\tilde{t} = K\Delta t$ that

$$\frac{y_1}{y_2} = \frac{1 + e^{\tilde{t}_0 - \Delta\tilde{t}}}{1 + e^{\tilde{t}_0}},$$

which is equivalent to

$$\begin{aligned}\frac{y_1}{y_2} &= \frac{1 + e^{\tilde{t}_0} - e^{\tilde{t}_0} + e^{\tilde{t}_0 - \Delta\tilde{t}}}{1 + e^{\tilde{t}_0}} \\ &= 1 + e^{\tilde{t}_0} \frac{e^{-\Delta\tilde{t}} - 1}{1 + e^{\tilde{t}_0}}.\end{aligned}$$

Similarly, we obtain that

$$\begin{aligned}\frac{y_2}{y_3} &= \frac{1+e^{\tilde{t}_0-2\Delta\tilde{t}}}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}\\ &= \frac{1+e^{\tilde{t}_0-\Delta\tilde{t}}-e^{\tilde{t}_0-\Delta\tilde{t}}+e^{\tilde{t}_0-2\Delta\tilde{t}}}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}\\ &= \frac{1+e^{\tilde{t}_0-\Delta\tilde{t}}}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}+\frac{-e^{\tilde{t}_0-\Delta\tilde{t}}+e^{\tilde{t}_0-2\Delta\tilde{t}}}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}\\ &= 1+e^{\tilde{t}_0-\Delta\tilde{t}}\frac{e^{-\Delta\tilde{t}}-1}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}.\end{aligned}$$

Hence, the growth metric $\Phi(y_1, y_2, y_3)$ defined in (6) becomes

$$\begin{aligned}\Phi(y_1,y_2,y_3) &= \left(e^{-\Delta\tilde{t}}-1\right)\left(\frac{e^{\tilde{t}_0-\Delta\tilde{t}}}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}-\frac{e^{\tilde{t}_0}}{1+e^{\tilde{t}_0}}\right)\\ &= \left(e^{-\Delta\tilde{t}}-1\right)\left(1-\frac{1}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}-1+\frac{1}{1+e^{\tilde{t}_0}}\right).\end{aligned}$$

We further simplify the growth metric $\Phi(y_1, y_2, y_3)$ as

$$\begin{aligned}\Phi(y_1,y_2,y_3) &= \left(e^{-\Delta\tilde{t}}-1\right)\left(\frac{1}{1+e^{\tilde{t}_0}}-\frac{1}{1+e^{\tilde{t}_0-\Delta\tilde{t}}}\right)\\ &= \left(e^{-\Delta\tilde{t}}-1\right)\left(\frac{1}{1+e^{\tilde{t}_0}}-e^{\Delta\tilde{t}}\frac{1}{e^{\tilde{t}_0}+e^{\Delta\tilde{t}}}\right).\end{aligned}$$

Thus, we obtain that

$$\begin{aligned}\Phi(y_1,y_2,y_3) &= \frac{e^{-\Delta\tilde{t}}-1}{1+e^{\tilde{t}_0}}-\frac{1-e^{-\Delta\tilde{t}}}{e^{\tilde{t}_0}+e^{\Delta\tilde{t}}}\\ &= \frac{e^{-\Delta\tilde{t}}-1}{1+e^{\tilde{t}_0}}-\left(-1+\frac{1+e^{\tilde{t}_0}}{e^{\tilde{t}_0}+e^{\Delta\tilde{t}}}\right),\end{aligned}$$

which finally simplifies to

$$\begin{aligned}\Phi(y_1,y_2,y_3) &= 1-\frac{1-e^{-\Delta\tilde{t}}}{1+e^{\tilde{t}_0}}-\frac{1+e^{\tilde{t}_0}}{e^{\tilde{t}_0}+e^{\Delta\tilde{t}}} \qquad (17)\\ &= \frac{e^{\tilde{t}_0}}{1+e^{\tilde{t}_0}}+\frac{1}{1+e^{\tilde{t}_0}}e^{-\Delta\tilde{t}}-\left(1+e^{\tilde{t}_0}\right)\frac{1}{e^{\tilde{t}_0}+e^{\Delta\tilde{t}}}.\end{aligned}$$

To express the growth metric $\Phi(y_1, y_2, y_3)$ as a power series around $\Delta\tilde{t} = 0$, we write the second addend in (17) as power series

$$e^{-\Delta\tilde{t}} = \sum_{n=0}^{\infty}\left(\Delta\tilde{t}\right)^n\frac{(-1)^n}{n!}. \qquad (18)$$

To express the third addend in (17) as power series, we first note that

$$\begin{aligned}e^{\tilde{t}_0}+e^{\Delta\tilde{t}} &= e^{\tilde{t}_0}+\sum_{n=0}^{\infty}\left(\Delta\tilde{t}\right)^n\frac{1}{n!}\\ &= e^{\tilde{t}_0}+1+\sum_{n=1}^{\infty}\left(\Delta\tilde{t}\right)^n\frac{1}{n!}.\end{aligned}$$

We normalise the first coefficient, corresponding to $\left(\Delta\tilde{t}\right)^0 = 1$, in the power series and obtain that

$$e^{\tilde{t}_0} + e^{\Delta\tilde{t}} = \left(e^{\tilde{t}_0} + 1\right) \sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n b_n,$$

where the power series coefficients b_n equal

$$b_n = \begin{cases} 1 & \text{if} \quad n = 0, \\ \frac{1}{n!} \frac{1}{e^{\tilde{t}_0}+1} & \text{if} \quad n \geq 1. \end{cases}$$

Thus, it holds that

$$\begin{aligned} \frac{1}{e^{\tilde{t}_0} + e^{\Delta\tilde{t}}} &= \frac{1}{1+e^{\tilde{t}_0}} \frac{1}{\sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n b_n} \\ &= \frac{1}{1+e^{\tilde{t}_0}} \sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n c_n. \end{aligned} \tag{19}$$

Here, the coefficient c_0 equals $c_0 = 1$ and, for $n \geq 1$, the coefficients c_n are given recursively by

$$c_n = -\sum_{l=0}^{n-1} c_l b_{n-l}.$$

In particular, it holds that

$$\begin{aligned} c_1 &= -c_0 b_1 \\ &= -\frac{1}{e^{\tilde{t}_0}+1}. \end{aligned} \tag{20}$$

With the two power series (18) and (19), we can express the growth metric $\Phi(y_1, y_2, y_3)$ in (17) as

$$\Phi(y_1, y_2, y_3) = \frac{e^{\tilde{t}_0}}{1+e^{\tilde{t}_0}} + \frac{1}{1+e^{\tilde{t}_0}} \sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n \frac{(-1)^n}{n!} - \sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n c_n.$$

Further simplification yields that

$$\Phi(y_1, y_2, y_3) = \frac{1}{1+e^{\tilde{t}_0}} \left(e^{\tilde{t}_0} + \sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n \left(\frac{(-1)^n}{n!} - \left(1+e^{\tilde{t}_0}\right) c_n \right) \right). \tag{21}$$

We explicitly write out the first two addends in the sum in (21) and obtain that

$$\begin{aligned} \sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n \left(\frac{(-1)^n}{n!} - \left(1+e^{\tilde{t}_0}\right) c_n \right) =& 1 - \left(1+e^{\tilde{t}_0}\right) c_0 \\ &+ \Delta\tilde{t} \left((-1) - \left(1+e^{\tilde{t}_0}\right) c_1 \right) \\ &+ \sum_{n=2}^{\infty} \left(\Delta\tilde{t}\right)^n \left(\frac{(-1)^n}{n!} - \left(1+e^{\tilde{t}_0}\right) c_n \right). \end{aligned}$$

With $c_0 = 1$ and (20), we obtain that

$$\sum_{n=0}^{\infty} \left(\Delta\tilde{t}\right)^n \left(\frac{(-1)^n}{n!} - \left(1+e^{\tilde{t}_0}\right) c_n \right) = -e^{\tilde{t}_0} + \sum_{n=2}^{\infty} \left(\Delta\tilde{t}\right)^n \left(\frac{(-1)^n}{n!} - \left(1+e^{\tilde{t}_0}\right) c_n \right).$$

Thus, (21) simplifies to

$$\Phi(y_1, y_2, y_3) = \frac{1}{1+e^{\tilde{t}_0}} \sum_{n=2}^{\infty} \left(\Delta\tilde{t}\right)^n \left(\frac{(-1)^n}{n!} - \left(1+e^{\tilde{t}_0}\right) c_n \right).$$

B Proof of Proposition 5

At any time t_i, where $i = 1, 2, 3$, the point y_i is on the hyperbolic tangent (2) if and only if

$$y_i + y_i e^{-K(t_i - t_0)} - y_\infty = 0.$$

Dividing by y_i yields that

$$e^{-K(t_i - t_0)} - \frac{1}{y_i} y_\infty + 1 = 0.$$

Thus, we arrive at a set of three non-linear equations

$$e^{Kt_0} e^{-Kt_i} - \frac{1}{y_i} y_\infty + 1 = 0, \quad i = 1, 2, 3. \tag{22}$$

To solve (22), we define two scalar unknowns as

$$a = e^{Kt_0} \tag{23}$$

and

$$b = e^{-Kt_2}. \tag{24}$$

Since $t_2 = \Delta t$ and $t_3 = 2\Delta t$, it holds that $t_3 = 2t_2$. Thus, we can express the second exponential in (22) as

$$e^{-Kt_i} = \begin{cases} 1 & \text{if} \quad i = 1, \\ b & \text{if} \quad i = 2, \\ b^2 & \text{if} \quad i = 3. \end{cases}$$

Then, we obtain from (22) a set of non-linear equations for the three unknowns a, b and y_∞ as

$$a - \frac{1}{y_1} y_\infty + 1 = 0, \tag{25}$$

$$ab - \frac{1}{y_2} y_\infty + 1 = 0, \tag{26}$$

$$ab^2 - \frac{1}{y_3} y_\infty + 1 = 0. \tag{27}$$

The first equation (25) yields that

$$y_\infty = y_1 (a + 1). \tag{28}$$

Combining (28) with the second equation (26) gives that

$$ab - \frac{y_1}{y_2} (a + 1) + 1 = 0,$$

from which we obtain that

$$b = \frac{1}{a} \left(\frac{y_1}{y_2} (a + 1) - 1 \right).$$

Hence, it holds that

$$b = \frac{1}{a}\left(\frac{y_1}{y_2} - 1\right) + \frac{y_1}{y_2}. \tag{29}$$

Combining the expressions for y_∞ and b in (28) and (29), respectively, with the third equation (27) yields that

$$a\left(\frac{1}{a}\left(\frac{y_1}{y_2} - 1\right) + \frac{y_1}{y_2}\right)^2 - \frac{y_1}{y_3}(a+1) + 1 = 0,$$

which is equivalent to

$$\frac{1}{a}\left(\frac{y_1}{y_2} - 1\right)^2 + 2\left(\frac{y_1}{y_2} - 1\right)\frac{y_1}{y_2} + a\frac{y_1^2}{y_2^2} - \frac{y_1}{y_3}(a+1) + 1 = 0.$$

Multiplication with a and rearranging gives that

$$a^2\left(\frac{y_1^2}{y_2^2} - \frac{y_1}{y_3}\right) + a\left(2\frac{y_1}{y_2}\left(\frac{y_1}{y_2} - 1\right) - \frac{y_1}{y_3} + 1\right) + \left(\frac{y_1}{y_2} - 1\right)^2 = 0. \tag{30}$$

The quadratic equation (30) has two solutions. The first solution is $a = -1$ leads to a contradiction, since a, defined in (23), is positive. The second solution of (30) is

$$a = -\frac{\left(\frac{1}{y_2} - \frac{1}{y_1}\right)^2}{\frac{1}{y_2^2} - \frac{1}{y_1 y_3}},$$

which is equivalent to

$$a = \frac{(y_1 - y_2)^2}{y_1 y_2}\frac{1}{\frac{y_2}{y_3} - \frac{y_1}{y_2}}.$$

Thus, we obtain with the definition of the growth metric $\Phi(y_1, y_2, y_3)$ in (6)that

$$a = \frac{(y_1 - y_2)^2}{y_1 y_2}\frac{1}{\Phi(y_1, y_2, y_3)}. \tag{31}$$

Since $y_1 > 0$ and $y_2 > 0$, the expression (31) for a is positive only if

$$\Phi(y_1, y_2, y_3) > 0.$$

Hence, if and only if (7) holds true, there is a solution for the unknown a, and, hence, for the logistic growth rate K and the inflection point t_0. From (31) and (28), we obtain the steady-state y_∞ as

$$y_\infty = y_1 + \frac{(y_1 - y_2)^2}{y_2}\frac{1}{\Phi(y_1, y_2, y_3)}.$$

From (29) and (31), it follows that the unknown b equals

$$b = \frac{y_1}{y_2} + \left(\frac{y_1}{y_2} - 1\right)\frac{y_1 y_2}{(y_1 - y_2)^2}\Phi(y_1, y_2, y_3),$$

which simplifies to

$$b = \frac{y_1}{y_2} + \frac{y_1}{y_1 - y_2} \Phi\left(y_1, y_2, y_3\right). \tag{32}$$

The definition of b in (24) implies that

$$K = -\frac{1}{t_2} \log\left(b\right),$$

which yields with (32) and $t_2 = \Delta t$ that

$$K = -\frac{1}{\Delta t} \log\left(\frac{y_1}{y_2} + \frac{y_1}{y_1 - y_2} \Phi\left(y_1, y_2, y_3\right)\right).$$

Finally, we obtain the inflection point t_0 from (23) as

$$\begin{aligned} t_0 &= \frac{1}{K} \log(a) \\ &= \frac{1}{K} \log\left(\frac{\left(y_1 - y_2\right)^2}{y_1 y_2} \frac{1}{\Phi(y_1, y_2, y_3)}\right), \end{aligned}$$

where the last equality follows from (31).

C Proof of Proposition 7

C.1 Condition Number of Estimating the Steady State

From the definition of the condition number $\kappa_1(t_{\text{obs}})$ in (13), we obtain that

$$\kappa_1(t_{\text{obs}}) = -\frac{\left(y_1 - y_2\right)^2}{y_2} \frac{1}{\Phi^2(y_1, y_2, y_3)} \frac{\partial \Phi(y_1, y_2, y_3)}{\partial y_3}.$$

The definition of the growth metric $\Phi(y_1, y_2, y_3)$ in (6) yields that

$$\frac{\partial \Phi(y_1, y_2, y_3)}{\partial y_3} = -\frac{y_2}{y_3^2}. \tag{33}$$

Thus, the condition number $\kappa_1(t_{\text{obs}})$ follows as

$$\kappa_1(t_{\text{obs}}) = \frac{\left(y_1 - y_2\right)^2}{y_3^2} \frac{1}{\Phi^2(y_1, y_2, y_3)}.$$

C.2 Condition Number of Estimating the Logistic Growth Rate

With (9), we define the condition number $\kappa_2(t_{\text{obs}})$ with respect to the growth rate estimate $\hat{K}(t_{\text{obs}})$ as

$$\kappa_2(t_{\text{obs}}) = \frac{\partial}{\partial y_3}\left(-\frac{1}{\Delta t} \log\left(\frac{y_1}{y_2} + \frac{y_1}{y_1 - y_2} \Phi\left(y_1, y_2, y_3\right)\right)\right),$$

where $\Delta t = t_{\text{obs}}/2$. Hence, it holds that

$$\kappa_2(t_{\text{obs}}) = -\frac{1}{\Delta t} \frac{1}{\frac{y_1}{y_2} + \frac{y_1}{y_1 - y_2} \Phi\left(y_1, y_2, y_3\right)} \frac{y_1}{y_1 - y_2} \frac{\partial}{\partial y_3} \Phi\left(y_1, y_2, y_3\right).$$

Thus, we obtain with (33) that

$$\kappa_2(t_{\text{obs}}) = \frac{1}{\Delta t} \frac{1}{\frac{y_1}{y_2} - 1 + \Phi\left(y_1, y_2, y_3\right)} \frac{y_2}{y_3^2},$$

which simplifies to

$$\kappa_2(t_{\text{obs}}) = \frac{1}{\Delta t} \frac{y_2^2}{y_3^2} \frac{1}{y_1 - y_2 + y_2 \Phi\left(y_1, y_2, y_3\right)}. \tag{34}$$

The expression (15) for the condition number $\kappa_2(t_{\text{obs}})$ follows from $\Delta t = t_{\text{obs}}/2$.

C.3 Condition Number of Estimating the Inflection Point

With (10), we define the condition number $\kappa_3(t_{\text{obs}})$ with respect to the inflection point estimate $\hat{t}_0(t_{\text{obs}})$ as

$$\kappa_3(t_{\text{obs}}) = \frac{\partial}{\partial y_3} \left(\frac{1}{K} \log \left(\frac{(y_1 - y_2)^2}{y_1 y_2} \frac{1}{\Phi(y_1, y_2, y_3)} \right) \right),$$

which becomes

$$\begin{aligned}\kappa_3(t_{\text{obs}}) = &- \frac{1}{K^2} \log \left(\frac{(y_1 - y_2)^2}{y_1 y_2} \frac{1}{\Phi(y_1, y_2, y_3)} \right) \frac{\partial K}{\partial y_3} \\ &- \frac{1}{K} \frac{1}{\frac{(y_1 - y_2)^2}{y_1 y_2} \frac{1}{\Phi(y_1, y_2, y_3)}} \frac{(y_1 - y_2)^2}{y_1 y_2} \frac{1}{\Phi^2(y_1, y_2, y_3)} \frac{\partial}{\partial y_3} \Phi(y_1, y_2, y_3).\end{aligned}$$

Thus, it holds that

$$\begin{aligned}\kappa_3(t_{\text{obs}}) = &- \frac{1}{K^2} \log \left(\frac{(y_1 - y_2)^2}{y_1 y_2} \frac{1}{\Phi(y_1, y_2, y_3)} \right) \frac{\partial K}{\partial y_3} \\ &- \frac{1}{K} \frac{1}{\Phi(y_1, y_2, y_3)} \frac{\partial}{\partial y_3} \Phi(y_1, y_2, y_3).\end{aligned}$$

With (10), (33) and (34), we obtain that

$$\begin{aligned}\kappa_3(t_{\text{obs}}) = &- \frac{1}{K} t_0 \frac{1}{\Delta t} \frac{y_2^2}{y_3^2} \frac{1}{y_1 - y_2 + y_2 \Phi\left(y_1, y_2, y_3\right)} \\ &+ \frac{1}{K} \frac{1}{\Phi(y_1, y_2, y_3)} \frac{y_2}{y_3^2},\end{aligned}$$

which simplifies to

$$\kappa_3(t_{\text{obs}}) = \frac{1}{K} \frac{y_2}{y_3^2} \left(\frac{1}{\Phi(y_1, y_2, y_3)} - \frac{t_0 y_2}{\Delta t} \frac{1}{y_1 - y_2 + y_2 \Phi\left(y_1, y_2, y_3\right)} \right).$$

The expression (16) for the condition number $\kappa_3(t_{\text{obs}})$ follows from $\Delta t = t_{\text{obs}}/2$.

D Proof of Proposition 8

D.1 Condition Number of Estimating the Steady State

From (14), we obtain that

$$\frac{1}{\kappa_1(t_{\text{obs}})} = \frac{y_3^2}{\left(y_1 - y_2\right)^2}\Phi^2(y_1, y_2, y_3). \tag{35}$$

We consider the terms in (35) separately. The logistic function $f(t)$ is differentiable. Thus, it holds that

$$f(t_{\text{obs}}) = f(0) + t_{\text{obs}} f'(0) + \mathcal{O}\left(t_{\text{obs}}^2\right)$$

as $t_{\text{obs}} \downarrow 0$. Since $y_1 = f(0)$ and $y_2 = f(t_{\text{obs}}/2)$, we obtain that

$$y_1 - y_2 = \mathcal{O}\left(t_{\text{obs}}\right). \tag{36}$$

Furthermore, it holds that $y_3 = f(t_{\text{obs}}) \to f(0) > 0$ as $t_{\text{obs}} \downarrow 0$, which implies that $y_3 = \mathcal{O}(1)$. Proposition 6 states that $\Phi^2(y_1, y_2, y_3) = \mathcal{O}\left(t_{\text{obs}}^4\right)$ when $t_{\text{obs}} \downarrow 0$. Thus, obtain from (35) that

$$\frac{1}{\kappa_1(t_{\text{obs}})} = \mathcal{O}\left(t_{\text{obs}}^2\right)$$

as $t_{\text{obs}} \downarrow 0$.

D.2 Condition Number of Estimating the Logistic Growth Rate

From (15), we obtain that

$$\frac{1}{\kappa_2(t_{\text{obs}})} = \frac{y_3^2}{2y_2^2} t_{\text{obs}} \left(y_1 - y_2 + y_2 \Phi\left(y_1, y_2, y_3\right)\right).$$

From (36), we obtain that $t_{\text{obs}}(y_1 - y_2) = \mathcal{O}\left(t_{\text{obs}}^2\right)$ as $t_{\text{obs}} \downarrow 0$. Furthermore, Proposition 6 implies that $t_{\text{obs}}\Phi(y_1, y_2, y_3) = \mathcal{O}\left(t_{\text{obs}}^3\right)$. Thus, we obtain that $1/\kappa_2(t_{\text{obs}}) = \mathcal{O}\left(t_{\text{obs}}^2\right)$ as $t_{\text{obs}} \downarrow 0$.

D.3 Condition Number of Estimating the Inflection Point

From (16), we obtain that

$$\frac{1}{\kappa_3(t_{\text{obs}})} = \left(\frac{1}{K}\frac{y_2}{y_3^2}\frac{t_{\text{obs}}\left(y_1 - y_2 + y_2\Phi\left(y_1, y_2, y_3\right)\right) - 2t_0 y_2 \Phi\left(y_1, y_2, y_3\right)}{t_{\text{obs}}\Phi(y_1, y_2, y_3)\left(y_1 - y_2 + y_2\Phi\left(y_1, y_2, y_3\right)\right)}\right)^{-1},$$

which is equivalent to

$$\frac{1}{\kappa_3(t_{\text{obs}})} = K\frac{y_3^2}{y_2}\frac{t_{\text{obs}}\Phi(y_1, y_2, y_3)\left(y_1 - y_2\right) + y_2 t_{\text{obs}}\Phi^2(y_1, y_2, y_3)}{t_{\text{obs}}\left(y_1 - y_2 + y_2\Phi\left(y_1, y_2, y_3\right)\right) - 2t_0 y_2\Phi\left(y_1, y_2, y_3\right)}. \tag{37}$$

From Proposition 6 and (36), we obtain that the numerator in (37) satisfies

$$t_{\text{obs}}\Phi(y_1, y_2, y_3)\left(y_1 - y_2\right) + y_2 t_{\text{obs}}\Phi^2(y_1, y_2, y_3) = \mathcal{O}\left(t_{\text{obs}}^4\right)$$

as $t_{\text{obs}} \downarrow 0$. Similarly, we obtain that, when $t_{\text{obs}} \downarrow 0$, the denominator in (37) satisfies

$$t_{\text{obs}}\left(y_1 - y_2\right) + t_{\text{obs}} y_2 \Phi\left(y_1, y_2, y_3\right) - 2t_0 y_2\Phi\left(y_1, y_2, y_3\right) = \mathcal{O}\left(t_{\text{obs}}^2\right).$$

Hence, we obtain from (37) that $1/\kappa_3(t_{\text{obs}}) = \mathcal{O}\left(t_{\text{obs}}^2\right)$ as $t_{\text{obs}} \downarrow 0$.